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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,201	04/17/2006	Claude Monneret	037150153	8802
22852 7590 06/27/2007 FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			EXAMINER HAVLIN, ROBERT H	
			ART UNIT 1609	PAPER NUMBER
			MAIL DATE 06/27/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/576,201	MONNERET ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Robert Havlin	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☒ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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**DETAILED ACTION**

**Status of the claims:** Claims 1-11 and 13 are currently pending. At filing, claims 2-11 were amended, claim 13 was added, and claim 12 was cancelled.

**Priority:** This application is a 371 of PCT/FR04/02218 09/01/2004 and claims foreign priority to FRANCE 0310367 filed on 09/02/2003.

**IDS:** The IDS of 11/6/2006 has been considered.

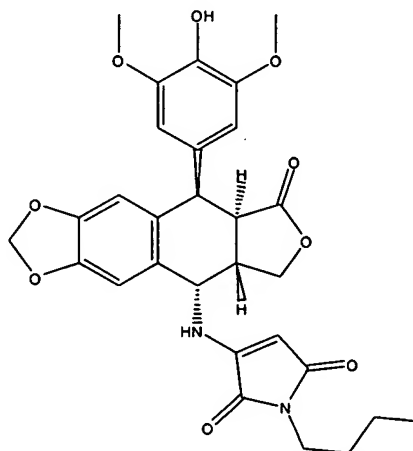
***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho et al. (J. Med. Chem. 1996, 36, 1383-1395) in view of Jensen et al. (PGPUB US 2003/0032625).

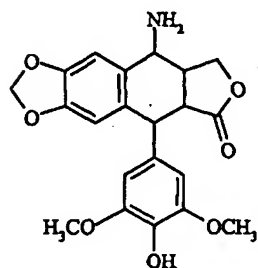
The claims read on a product including the species of



3-[[[(5S,5aS,8aR,9R)-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxo-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl]amino]-1-butyl-1H-pyrrole-2,5-dione

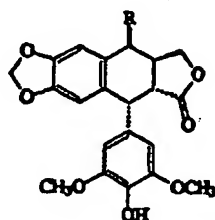
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As well as modifications of the butyl group to include methyl and aryl which may be substituted and compositions thereof. In addition, there is a claim to a method of making the aforementioned compounds by coupling a maleimide derivative with



Determination of the scope and content of the prior art

**Cho et al.** teaches podophyllotoxin derivatives for the treatment of cancer including a

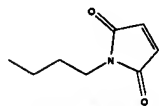


genus of compounds of the formula

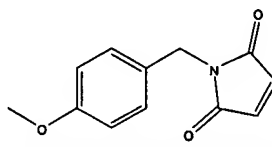
wherein R is an amino group

substituted with various cyclic and heterocyclic groups while keeping the structure depicted above constant. The reference teaches the motivation to modify the R group in order to optimize the antitumor antitopoisomerase activity of the compound as driven by SAR (page 1383, col. 2, first para.).

**Jensen et al.** teaches maleimide compounds as topoisomerase inhibitors including



1-Butyl-pyrrole-2,5-dione



1-(4-Methoxy-benzyl)-pyrrole-2,5-dione

on page 20 paragraph 209; para. 210. The reference also teaches the use of a halogenated form of maleimide to couple to amines.

Differences:

Differences between the prior art and the claims

The maleimide of Jensen et al. is not attached to an amine at the Cho et al.'s R, they are separate molecules whereas in the instant claims they are attached in one molecule. Furthermore, the claim 6 requires R2 is a methyl group.

Finding of prima facie obviousness – rationale and motivation

Both references are for treating cancer through affecting topoisomerase and the combination of the two factors for the same purpose of the instant invention is an obvious combination. Cho et al. teaches the optimization of the substituent at the R position therefore suggesting a motivation to modify the heterocyclic group to a factor that would reasonably be expected to inhibit topoisomerase and further have antitumor properties. One of ordinary skill in the art would reasonably be expected to be aware of the antitumor activity of both compounds due to their identical field and problem to be solved. In addition, since the Cho et al. teaches the motivation to modify the R position one of ordinary skill in the art would be motivated to modify the substituent to further increase the antitumor activity of the resulting compound and optimize it by altering the N position of maleimide as was done in Jensen et al.

Methods of making the compound described above would also be obvious to one of ordinary skill in the art. The claim teaches the use of a halogenated form of the maleimide to couple it to the amine of Cho et al.'s R group in the same manner as described in Jensen et al. Furthermore, the use of "traditional" protecting groups are well known in the art as indicated by the applicant in the claims and specification.

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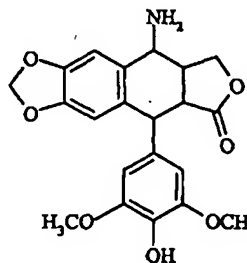
Therefore the method of making the compound is also obvious as are compositions thereof and methods of using for the identical purposes of Jensen et al and Cho et al.

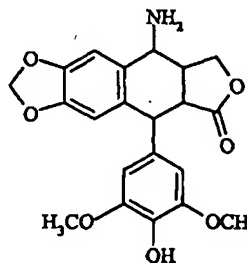
***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the



invention. Applicants state that the starting material of  was used without any specific reference to any description of how to make the starting material required to make and use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior

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art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to a chemical compound. Thus, the claims taken together with the specification imply that one of skill in the art can make or has readily available the compound referred to above without any specific teachings from other sources.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

The state of the art in chemical synthesis can be somewhat unpredictable when the number of functional groups is such that the groups can interfere or have side reactions with the usual methods employed.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for no example of making the starting material.

*(8) The quantity of experimentation necessary:*

Considering the state of the art and the unpredictability in the art, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims. The examiner invites the applicant to provide evidence that the starting material is readily available or provide a teaching that would sufficiently enable one of ordinary skill in the art to make and use the invention.

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3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 5-8, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The definition of Y in claim 1 as "HN-NH or N-R2" without any guidance as to where the bonds are formed within the maleimide ring would be confusing to one of ordinary skill in the art as to what the applicant regards as their invention. Similarly in claims 5-8 the definition of Y is ambiguous with respect to where the bonds occur. On page 10 of the amended claims, claim 10 defines R3 and T with language of "are such as defined in the formula (I)" when there is no definition of R3 and T in formula (I). This same problem occurs on page 10 for Y and R4. On page 10 there is no formula (I/a) or (I/b) defined. In addition, in two places on page 11, R1, R3, R4, Y and G are defined "are such as previously defined" which does not distinctly claim the invention due to a lack of any specific reference.

### ***Conclusion***

All claims are rejected.

### **Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.



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If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert Havlin  
Examiner

RH

  
JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER